Complete Summary

GUIDELINE TITLE

Liposomal anthracyclines in the management of patients with HIV-positive Kaposi´s sarcoma.

BIBLIOGRAPHIC SOURCE(S)

Systemic Treatment Disease Site Group. Iscoe N, Bramwell V, Charette M, Oliver T, Zanke B. Liposomal anthracyclines in the management of patients with HIV-positive Kaposi's sarcoma [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2004 Jun [online update]. 14 p. (Practice guideline report; no. 12-8). [15 references]

GUIDELINE STATUS

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COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Human immunodeficiency virus (HIV)-positive Kaposi´s sarcoma

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Infectious Diseases
Oncology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To evaluate whether liposomal anthracycline therapy has advantages over standard combination therapy for patients with human immunodeficiency virus (HIV)-positive Kaposi´s sarcoma who have aggressive cutaneous or visceral disease

TARGET POPULATION

Patients with human immunodeficiency virus (HIV)-positive Kaposi´s sarcoma and good performance status (Eastern Cooperative Oncology Group [ECOG] 0–2) who have progressive cutaneous disease despite prior treatment with interferon and/or vinblastine, or who have visceral disease that is symptomatic or progressive

INTERVENTIONS AND PRACTICES CONSIDERED

Treatment

1. Liposomal daunorubicin
2. Liposomal doxorubicin alone or combined with bleomycin and vincristine

MAJOR OUTCOMES CONSIDERED

- Survival
- Time-to-treatment failure
- Response rates
- Adverse effects
- Quality of life

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Original Guideline

The literature was searched using the MEDLINE (Ovid) (1966 through August 2002), CANCERLIT (Ovid) (1983 through July 2002), and Cochrane Library (Issue 3, 2002) databases. In addition, the Physician Data Query clinical trials database, and abstracts published in the conference proceedings from the meetings of the American Society of Clinical Oncology (1995–2002), and the European Society for Medical Oncology (1998, 2000) were searched for reports of new or ongoing trials. The Canadian Medical Association Infobase and the National Guideline Clearinghouse databases were searched for relevant clinical practice guidelines. Relevant articles and abstracts were selected and reviewed by one member of the Systemic Treatment Disease Site Group (STDSG) and methodologists, and the reference lists from these sources were searched for additional trials.

The literature search combined the disease specific terms (sarcoma, kaposi/ or kaposi:.tw. and HIV/ or HIV.mp. or HIV infections/ or human immunodeficiency virus.tw. or AIDS/) with treatment specific terms (drug therapy/ or anthracyclines/ or anthracyclines.mp. or liposome:.and doxorubicin.mp. or liposome:.and daunorubicin.mp or doxil.tw. or caelyx.tw. or liposom:.mp. or daunoxome.tw.) with search specific terms for the following study designs: practice guidelines, systematic reviews or meta-analyses, reviews, randomized controlled trials, and clinical trials.

June 2004 Update

The original literature search has been updated using MEDLINE (September 2002 through June 2004), EMBASE (September 2002 through June 2004), the Cochrane Library (Issue 2, 2004), the Physician Data Query database, the Canadian Medical Association Infobase, and the National Guideline Clearinghouse, as well as abstracts published in the proceedings of the meetings of the American Society of Clinical Oncology (2004), and the European Society for Medical Oncology (2002). Article bibliographies and personal files were also searched to June 2004 for evidence relevant to this practice guideline report. Please note that CANCERLIT is no longer included in update searches: results from an internal Practice Guidelines Initiative (PGI) project indicated that the overlap with MEDLINE is 100%, making CANCERLIT database searches redundant.

Inclusion Criteria

Articles were selected for inclusion in this systematic review of the evidence if they met the following criteria:

1. Randomized controlled trials (RCTs) comparing a liposomal anthracycline regimen to observation, placebo, or another chemotherapy regimen for the treatment of human immunodeficiency virus (HIV)-positive Kaposi´s sarcoma (KS)
2. Reported data on outcomes of interest including survival, time-to-treatment-failure, response rates, adverse effects, and quality of life
3. Trials reporting on patients with aggressive cutaneous or visceral HIV-positive KS

Exclusion Criteria

1. Phase I and II studies were not considered, because of the availability of randomized controlled trials.
2. Letters, editorials, and review articles were not included in this report.
3. Papers published in a language other than English were not considered.
4. Trials including only patients with non-aggressive cutaneous KS were not considered.

NUMBER OF SOURCE DOCUMENTS

Five randomized trials were identified

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The treatment and control arms were different in each of the eligible reviewed trials. The experimental arms of the reviewed trials varied, with three trials using liposomal doxorubicin, and the fourth examining liposomal daunorubicin. The control arms also varied, with the chemotherapy regimens consisting of a combination of doxorubicin, bleomycin, and vincristine in one trial and liposomal doxorubicin, bleomycin, and vincristine in one trial. Therefore, it was judged inappropriate by the Systematic Treatment Disease Site Group to pool the data by performing a meta-analysis.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

A preliminary draft of this practice guideline report was circulated to the members of the Systemic Treatment Disease Site Group (STDSG) for comment. The discussions at the Disease Site Group (DSG) meetings highlighted the need to identify the patient group to whom this guideline was directed. The discussion also focused at some length on the interpretation of the data. Special care was taken to ensure that the information was conveyed in a manner that would be helpful to practitioners. As a result of these discussions, the initial draft of the practice-guideline-in-progress was modified. The modified version was recirculated to the STDSG for further comments before being sent for feedback from physicians

involved in the care of patients with human immunodeficiency virus (HIV)-positive Kaposi´s sarcoma.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Table 4 in the original guideline document outlines the cost per week (in Canadian dollars) for treating an average patient with either a liposomal anthracycline regimen or a combination regimen of doxorubicin, bleomycin, and vincristine. The acquisition costs reflect only a component of the costs of delivering therapy. Costs associated with pharmacy workload and chemotherapy administration need to be considered, but are beyond the scope of this report. If liposomal anthracycline therapy is being considered, the direct cost of liposomal daunorubicin appears more attractive to that of liposomal doxorubicin. However, for an accurate comparison, detailed cost-effectiveness analyses based on Canadian data are needed. Unfortunately no such analyses were identified in the literature.

Two cost-effectiveness analyses, one Swedish and the other American, were identified. The authors computed the projected cost (in American dollars) of the two liposomal formulations to achieve similar rates of response as reported in two of the identified randomized trials. The authors concluded that despite higher acquisition costs, the costs for liposomal doxorubicin were actually much lower than those for liposomal daunorubicin. Given the current price differences between the two liposomal 11 formulations, the results of the ongoing randomized trial comparing the two formulations will hopefully clarify the relative merits of the two agents.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Practitioner feedback was obtained through a mailed survey of nine practitioners in Ontario (seven medical oncologists and two hematologists). The survey consisted of 21 items evaluating the methods, results, and interpretive summary used to inform the draft recommendations outlined and whether the draft recommendations above should be approved as a practice guideline. Written comments were invited. Follow-up reminders were sent at two weeks (post card) and four weeks (complete package mailed again). The results of the survey were reviewed by the Systemic Treatment Disease Site Group (DSG).

The practice guideline report was circulated to members of the Practice Guidelines Coordinating Committee (PGCC) for review and approval. Nine of eleven members of the PGCC returned ballots. Five PGCC members approved the practice guideline report as written, and four members approved the guideline conditional on the Systemic treatment DSG addressing specific concerns.

The practice guideline report was subsequently approved by the Systemic Treatment DSG and the Practice Guidelines Coordinating Committee.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The use of conventional combination chemotherapy or single-agent liposomal anthracycline therapy represent reasonable treatment options in the management of patients with human immunodeficiency virus (HIV)-positive Kaposi´s sarcoma.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are supported by randomized controlled trials.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Increased understanding of the efficacy of liposomal anthracycline therapy compared with standard combination therapy for patients with human immunodeficiency virus (HIV)-positive Kaposi´s sarcoma who have aggressive cutaneous or visceral disease

POTENTIAL HARMS

In terms of adverse events, rates of severe toxicity and opportunistic infection appear to be roughly equivalent between liposomal anthracycline therapy and conventional chemotherapy. However, it is clear that vincristine and bleomycin contribute significantly to toxicity, notably neurotoxicity. Therefore, if patients have neuropathy, or are at significant risk for neurotoxicity, the use of a liposomal anthracycline agent is a very attractive alternative to the commonly used combination regimen of doxorubicin, bleomycin, and vincristine. While not all patients with Kaposi´s sarcoma develop neurotoxicity on conventional chemotherapy, many are on antiretroviral regimens that may cause peripheral nerve damage, and many develop signs and symptoms of neurotoxicity as a result of these therapies.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- Many antiviral regimens used in the treatment of human immunodeficiency virus (HIV) cause peripheral nerve damage. In patients with HIV-positive Kaposi´s sarcoma, the risk of neuropathic toxicity appears to be greater with vinca alkaloid-containing conventional treatment regimens than with single-agent liposomal anthracyclines. Therefore, if patients have neuropathy, or are at significant risk for neurotoxicity, liposomal anthracycline therapy may be preferable to conventional combination chemotherapy.
- Care has been taken in the preparation of the information contained in this document. Nonetheless, any person seeking to apply or consult these guidelines is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or warranties of any kind whatsoever regarding their content or use or application and disclaims any responsibility for their application or use in any way.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 Jun

GUIDELINE DEVELOPER(S)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

The Practice Guidelines Initiative (PGI) is the main project of the Program in Evidence-based Care (PEBC), a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

SOURCE(S) OF FUNDING

Cancer Care Ontario
Ontario Ministry of Health and Long-Term Care

GUIDELINE COMMITTEE

Provincial Systemic Treatment Disease Site Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

For a current list of past and present members, please see the Cancer Care Ontario Web site.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Members of the Systemic Treatment Disease Site Group (STDSG) disclosed potential conflict of interest information.

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GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Liposomal anthracyclines in the management of patients with HIV-positive Kaposi's sarcoma. Summary. Toronto (ON): Cancer Care Ontario. Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.
- Browman GP, Levine MN, Mohide EA, Hayward RSA, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. J Clin Oncol 1995;13(2):502-12.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on September 27, 2004. The information was verified by the guideline developer on October 20, 2004.

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Date Modified: 9/25/2006